UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte
RAJIV PARIKH,
BHAIRAVI PARIKH and ANDREW NEWMAN

Appeal 2007-1820
Application 10/659,408
Technology Center 1600

Decided: September 4, 2007

Before TONI R. SCHEINER, DEMETRA J. MILLS, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 18-27. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF CASE

The claimed invention relates to methods of treating respiratory disorders, such as asthma. "Asthma is a chronic condition in which allergens or other triggers cause changes in a subject's airways, resulting in coughing, wheezing, and shortness of breath (dyspnea)" (Spec. ¶ 2).

"Inflammation is present in the lungs of all patients with asthma, even when they are not experiencing symptoms. When the airways become inflamed, the body responds by releasing nitric oxide into the local environment" (Spec. ¶ 3).

"Managing asthma is an ongoing challenge for clinicians, in large part because it has been difficult to accurately assess a patient's asthmatic status" (Spec. ¶ 4). "The fundamental problem with these traditional asthma monitoring techniques is their inability to directly measure airway inflammation. Given the shortcomings of the current asthma management techniques, there is a need for new procedures that can be tied more directly to airway inflammation" (Spec. ¶ 7). "The present invention is a method of managing asthma and other airway disorders using eNO [exhaled nitric oxide] values" (Spec. ¶ 13).

There are two rejections on appeal:

1) Claims 18-27 stand rejected under 35 U.S.C. § 103(a) as obvious over Moilanen (US Pat. Pub. App. 2002/0193698 A1, published Dec. 19, 2002) in view of Kharitonov (*Monaldi Arch. Chest Dis.*, 51(6): 533-537, 1996) (Answer 3); and

2) Claims 18-24 stand rejected under 35 U.S.C. § 103(a) as obvious over Hampton (US Pat. Pub. App. 2003/0073919 A1, published Apr. 17, 2003) in view of Moilanen (Answer 8).

The claims within each rejection stand or fall together because Appellants have not provided separate reasons for the patentability of any individual claim, but instead argue the claims in each rejection as a single group. We select claim 18 as representative of each rejection to decide all

issues in this appeal. *See* 37 C.F.R. § 41.37(c)(1)(vii). Claim 18 reads as follows:

> A method for managing a respiratory condition characterized by inflammation of air passageways in a subject who is undergoing treatment for said condition, said method comprising:
>
> (a) establishing a baseline range of nitric oxide concentration in said exhaled breath, said baseline range representing said condition being under control in said subject;
>
> (b) measuring nitric oxide concentrations in a series of samples of exhaled breath taken from said subject at a measurement frequency of at least three times per week over a period of at least seven days, and comparing said nitric oxide concentrations so measured to said baseline range;
>
> (c) if said nitric oxide concentrations so measured are within said baseline range or deviate therefrom by less than 5 ppb based on an exhalation rate of 50 mL/sec, or if said nitric oxide concentrations exceed the upper limit of said baseline range by 5 ppb or more based on an exhalation rate of 50 mL/sec but indicate a decreasing trend, continuing said treatment without change; and
>
> (d) if said nitric oxide concentrations so measured exceed said upper limit by 5 ppb or more without indicating a decreasing trend, modifying said treatment and measuring nitric oxide concentrations in further samples of exhaled breath at said frequency for at least five days and repeating step (c) as necessary to bring said nitric oxide concentration within said baseline range or deviating therefrom by less than 5 ppb based on an exhalation rate of 50 mL/sec.

DISCUSSION

Moilanen in view of Kharitonov

Claims 18-27 stand rejected under 35 U.S.C. § 103(a) over Moilanen in view of Kharitonov.

Findings of Fact

Moilanen

1. Moilanen teaches a method for measuring NO in exhaled air (Moilanen, at [0001]).

2. Moilanen reports that levels of exhaled NO are higher in patients with asthma and alveolitis as compared to healthy persons (Moilanen, at [0026] and Fig. 2).

3. Moilanen "also studied the effect of anti-inflammatory drug treatment on . . . NO output in patients with asthma . . . 16 patients with asthma started 8 weeks of treatment with inhaled glucocorticoids to suppress their asthmatic airway inflammation. . . . [T]here was a significant decrease in bronchial NO flux already after one week of anti-inflammatory treatment, and after 8 weeks the bronchial NO flux of these 16 asthmatics was similar to healthy controls. The decrease in bronchial NO flux during the drug treatment took place simultaneously with decrease in asthmatic symptoms and improvement of lung function of these subjects" (Moilanen, at [0030]).

4. "The results . . . suggest that the present method can be used to follow-up drug treatment of inflammatory lung diseases and provide means to assess the efficacy of such treatment" (Moilanen, at [0031]).

Kharitonov

5. Kharitonov teaches that exhaled nitric oxide (NO) is a marker of airway inflammation (Kharitonov, at 533 ("Nitric oxide in exhaled air is a new

marker of airway inflammation"), 534 ("Functional importance of exhaled NO"), and 535 ("There is now persuasive evidence that levels of NO are increased in association with airway inflammation and are decreased with anti-inflammatory therapy").

6. A study is described by Kharitonov in which patients with asthma "showed a progressive reduction in exhaled NO down to normal levels after 3 weeks of therapy" with inhaled budesonide (Kharitonov, at 535, col. 2).

7. Kharitonov states that "[b]ecause exhaled NO is reduced by anti-inflammatory treatments, it may be of use in monitoring whether therapy is adequate" (Kharitonov, at 536, col. 1).

8. The NO measurements can "be performed repeatedly" (Kharitonov, at 536, col. 1).

9. "However, the measurement is not specific, and exhaled NO is increased in inflammation due to asthma, bronchiectasis . . . , and respiratory tract infections. . . . This means that absolute values are less important than serial measurements in individual patients" (Kharitonov, at 536, col. 1).

Analysis

The Examiner contends:

> It would have been obvious . . . to combine the teachings of Moilanen and Kharitonov, because both references teach the utility of monitoring exhaled nitric oxide levels as a metric to evaluate anti-inflammatory treatment. . . . It would have been apparent to a skilled artisan that one would use the curve for exhaled nitric oxide (NO) of healthy patients provided by Moilanen as a baseline to ascertain the effectiveness of treatment because the achievement of normative exhaled nitric oxide levels is obviously a goal of these therapeutic methods. It would have been apparent that a skilled artisan would use a patient's initial eNO measurements as a baseline [claim 18, step

> (a)] for comparison to ascertain whether treatment was effective.

(Answer 7.) The Examiner also contends that it would have been obvious to have used "trends" as recited in claim 18, steps (c) and (d), to modify drug treatment because Kharitonov's description of "progressive" changes in eNO implies an observed trend that would be monitored to ascertain the efficacy of drug therapy and determine when therapy should be adjusted (Answer 7-8).

It is the Examiner's burden to establish prima facie obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). Obviousness requires a teaching that all elements of the claimed invention are found in the prior art and "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007). In our opinion, the Examiner has sustained his burden of establishing prima facie obviousness by providing a teaching of all elements of the claimed subject matter and a logical reason that would prompted one skilled in the art to combine them.

Appellants contend that Moilanen does not teach a baseline as it is used in their invention (Appeal Br. 6; Reply Br. 2). They argue that baseline utilized in Moilanen "is averaged over 57 disease and 57 healthy patients rather than on a specific patient on which the information is to be in used in the practice of Appellants' invention" (Reply Br. 2). Appellants also contend that "neither [Moilanen] nor [Kharitonov] disclose or suggest the frequency of the measurement needed to establish the baseline, or the frequency or number of measurements over any period of time to determine the amount or direction of the change in measured NO levels, much less any

tailoring of modifications of the treatment . . . [as] recited in the claims on appeal (Appeal Br. 7). We do not agree that the Examiner erred in the findings or the conclusion that claim 18 is obvious over the cited prior art.

Kharitonov states that the exhaled NO "measurement is not specific, and exhaled NO is increased in inflammation due to asthma, bronchiectasis . . . , and respiratory tract infections. . . . This means that absolute values are less important than serial measurements in individual patients" (FF 9; Kharitonov, at 536, col. 1). An "absolute value," as referred to by Kharitonov, would be the type of exhaled NO curve generated for healthy persons by Moilanen (FF 2; *see* Moilanen, at [0026] and Fig. 2 showing curves for healthy and diseased persons). Kharitonov states that such a curve would be inappropriate to monitor lung inflammation in asthmatics because exhaled NO levels are affected by other types of inflammation. Thus, Kharitonov recommends repeated serial measurements in the same patient. Kharitonov does not expressly say that the serial measurements should be of baseline normal activity, but it does describe monitoring therapy until a normal level of exhaled NO is observed (FF 6; Kharitonov, at 535, col. 2) and to determine when therapy is adequate (FF 7; Kharitonov, at 536, col. 1). In this context and with Kharitonov's emphasis that NO measurements can "be performed repeatedly" (FF 8; Kharitonov, at 536, col. 1), it would be logical that baseline normal NO concentrations would be determined in order to know when therapy was effective, i.e., efficacy is achieved when the individual patient's NO levels are restored to the patient's own baseline levels. Thus, we conclude that the Examiner was correct in finding that Kharitonov teaches step (a) of claim 18 of "establishing a baseline range of nitric oxide concentration in said exhaled breath, said

baseline range representing said condition being under control in said subject."

We agree with Appellants (*see supra* at p. 6; Reply Br. 2) that, in Moilanen's study which looked at levels of NO in healthy persons and patients with asthma and alveolitis (Moilanen, at [0029]), a "baseline range representing said condition being under control in said subject" was not established (Claim 18). However, the purpose of this study was to establish that lung inflammation was associated with elevated levels of NO, not to monitor the disease.

However, in a different study aimed at determining the effect of anti-inflammatory treatment on asthma, Moilanen states "there was a significant decrease in bronchial NO flux already after one week of anti-inflammatory treatment" (FF 3; Moilanen, at [0030]). This indicates that Moilanen compared NO levels in the same patient before and after treatment as a way of assessing drug efficacy. In other words, Moilanen assessed a patient's "baseline range representing said condition being under control" as recited in step (a) of claim 18. Following the description of this study, Moilanen concludes that "the present method can be used to follow-up drug treatment of inflammatory lung diseases and provide means to assess the efficacy of such treatment" (FF 4; Moilanen, at [0031]). We agree with the Examiner that, based on these teachings, "[i]t would have been apparent that a skilled artisan would use a patient's initial eNO measurements as a baseline for comparison to ascertain whether treatment was effective" (Answer 7) as required by claim 18. Appellants have not persuaded us that the Examiner erred in this conclusion.

It is undisputed that the prior art teaches that the levels of exhaled NO may be used to monitor the efficacy of anti-inflammatory treatment (FF 1, 7). In view of Kharitonov's teaching about the value of serial and repeated measurements (FF 8, 9), it is our strong opinion that it would have been obvious to use an individual baseline to assess drug efficacy and determine whether the treatment regime should be modified based on changes in it as recited in steps (b) through (d) of claim 18.

The cited prior art does not disclose the claimed "measurement frequency of at least three times per week over a period of at least seven days" and using deviations of less or more than "5 ppb or more based on an exhalation rate of 50 mL/sec" ("trends") to determine when to modify treatment as recited in steps (c) and (d) of claim 18.

However, we agree with the Examiner that "achievement of normative exhaled nitric oxide levels is . . . a goal of these therapeutic methods," thus making it obvious to make repeated measurements over time to determine the efficacy of therapy. Moilanen explicitly states that its method can be used to "follow-up drug treatment" (FF 4) and Kharitonov describes the "progressive reduction in exhaled NO" (FF 6), both indicating that the NO levels are measured over time. Choosing the particular intervals when to measure NO, such as "at least three times per week over a period of at least seven days" or "for at least five days" as recited in steps (b) and (d), respectively, of claim 18, appears to be nothing more than routine optimization of a known results-effective variable. "[I]t is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* also *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (C.C.P.A. 1980)

("[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art."); *Pfizer Inc. v. Apotex Inc.*, 480 F.3d. 1348, 1368, 82 USPQ2d 1321, 1335-36 (Fed. Cir. 2007). Appellants urge that the claimed time periods are critical (Appeal Br. 6), but they have provided no evidence of it. Arguments of counsel cannot take the place of evidence lacking in the record. *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 593, 44 USPQ2d 1610, 1615 (Fed. Cir. 1997).

In regard to the limitation in claim 18 that therapy is modified when deviations of more than "5 ppb based on an exhalation rate of 50 mL/sec" are observed, we likewise conclude that choosing the specific values at which to modify therapy is routine optimization well within the average level of skill in the art. *See* above *Aller*, 220 F.2d at 456, 105 USPQ at 235. Moreover, Moilanen states that its method can be used to "follow-up drug treatment" (FF 4) and Kharitonov suggests NO may be of use "in monitoring whether therapy is adequate" (FF 7). While neither expressly states that therapy should be modified when monitoring shows a rise in NO levels, what else could have been meant? The purpose of monitoring therapy is to determine when it's not working so the physician can intervene. Physicians – who are the persons of skill in the art in this field – conventionally adjust therapy in response to a patient's condition.

For the foregoing reasons, we conclude that the Examiner did not err in finding claims 18-27 as obvious over Moilanen in view of Kharitonov. The rejection is affirmed.

Rejection over Hampton and Moilanen

Claims 18-27 stand rejected under 35 U.S.C. § 103(a) as obvious over Hampton in view Moilanen (Answer 8).

Findings of Fact

10. Hampton teaches "techniques for identifying and guiding treatment for medical conditions, based upon the carbon dioxide concentration in the patient's breath" (Hampton, Abstract).

11. Hampton describes its technique as useful "for rapidly and reliably distinguishing obstructive lung disease from restrictive lung disease" (Hampton, at [0010]).

12. "To distinguish obstructive lung disease from restrictive lung disease, the invention employs measurements of carbon dioxide in the breath of the patient" using a device such as a capnograph (Hampton, at [0011]).

13. The measurements taken by a capnograph are represented by a capnogram (Hampton, at [0011]).

14. "The shape of the curve that follows carbon dioxide concentration is correlated with the ventilatory status of the patient" ((Hampton, at [0012]).

15. "[T]he invention quickly provides information to a health professional to guide treatment of the patient. . . . [T]he invention rapidly and reliably distinguishes obstructive lung disease from restrictive lung disease . . . [T]he invention may . . . be brought to the patient by an emergency medical professional. As a result, the ventilatory status of the patient may be assessed quickly" (Hampton, at [0016]).

16. "Memory . . . may store data that are characteristic of obstructive lung disease and . . . of restrictive lung disease. Processor 82 may correlate the

measurements of the concentration of carbon dioxide from the patient with the characteristic curves. When the correlation exceeds a preselected threshold value, processor 82 may determine that the data support a diagnosis of obstructive lung disease or restrictive lung disease" (Hampton, at [0046]).

Analysis

The Examiner states that Hampton teaches using exhaled carbon dioxide to monitor the effectiveness and guide treatment of respiratory disorders (Hampton, at Abstract and [0015]) (Answer 8-9). The Examiner contends that "[i]t would have been apparent to a skilled artisan that Hampton's teachings of comparing the concentration of carbon dioxide in breath to a characteristic curve could be modified to compare a patient's exhale nitric oxide measurements to characteristic curves (i.e. baselines) to evaluate treatment efficacy" (Answer 10).

The Examiner has the burden of establishing a reason to have modified the prior art to arrived at the claimed invention. In our opinion, the Examiner has not set forth sufficient evidence to establish prima facie obviousness of the claimed subject matter. In particular, the Examiner has not provided an adequate reason that would have prompted one skilled in the art to have modified Hampton in view of Moilanen to achieve the claimed invention.

The baseline described by Hampton is not "representing said [respiratory] condition being under control in said subject" as recited in claim 18. Instead, Hampton's "baseline" – if it could be even called that – is a standard curve of a single breath whose shape is diagnostic of either obstructive lung disease or restrictive lung disease (FF 14, 16). A patient

having breathing difficulty is instructed to breath into a capnograph which generates a curve plotting the concentration of carbon dioxide over the course of the breath (FF 12, 14, and 15). The curve is called a capnogram (FF 13). The patient's capnogram is compared to the standard curve, which may be stored in the memory of the device, to determine whether the patient is suffering from obstructive or restrictive lung disease (FF 15, 16). The Examiner does not explain why it would be apparent from Hampton's teaching of comparing a one-time breath to a standard curve, to use a baseline from the same patient in which the condition is "under control" as required by claim 18. Because Hampton's device is for diagnosis, including during medical emergencies, we see no reason, or even opportunity, to use the patient's baseline normal ("under control") for the comparison. Hampton explains that "[e]very day, patients with difficulty breathing seek medical help. In such cases, the patients may complain of shortness of breath, but may have no idea as to the cause of the condition" (Hampton, at [0002]). Thus, because the patient's need for the device arises during an unexpected medical emergency (FF 15), there would have been no reason to have obtained the patient's normal capnograph baseline in advance.

In addition to this, Hampton, unlike Kharitonov as discussed above, does not describe repeated measurements of carbon dioxide over time and thus does not suggest "measurement frequency of at last three times per week over a period of seven days" as recited in claim 18. The Examiner does not explain how the claimed frequency measurement is suggested by the combination of Hampton in view of Moilanen, and thus has not met the burden of establishing the obviousness of this claim limitation.

For the foregoing reasons, we concluded that the Examiner erred in finding claims 18-24 obvious over Hampton with Moilanen. The rejection is reversed.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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